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Integrating Phage Therapy into Western Medicine

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Introduction

The World Health Organization reported in 2000 concerning the “growing threat of antimicrobial resistance.” Bacteriophages are highly specific viruses that only infect a small range of bacteria. Using bacteriophages to treat bacterial infections is called phage therapy. Research in phage therapy began in the early 20th century until the introduction of antibiotics. While the US and other Western nations moved away from phage therapy, the Soviet Union and its satellite nations continued to research phages. As phage therapy was a standard of care in the countries it was used in, the studies done were not double-blind, placebo controlled and not applicable to the standards of the Food and Drug Administration (FDA) and European Medicines Agency (EMA).

Mechanics of Phage Growth

Viruses replicate by inserting their genome into bacteria to replicate and express their DNA (Figure 1). A phage can be either lysogenic or lytic (Figure 2). A lysogenic phage will initiate lysis, cell death, immediately after all the phage parts are made and assembled. A lysogenic phage genome will remain latent in the bacteria’s genome for several generation until lysis is induced.

Phage therapy involves give a patient a does of phage which would then replicate at the site of infection (Figure 3)until there was no longer a sufficient host to infect. Phage therapy can be applied after identifying the bacteria and matching the bacteria to a phage. The other way involved giving the patient a cocktail of phage with a wide host ranges.

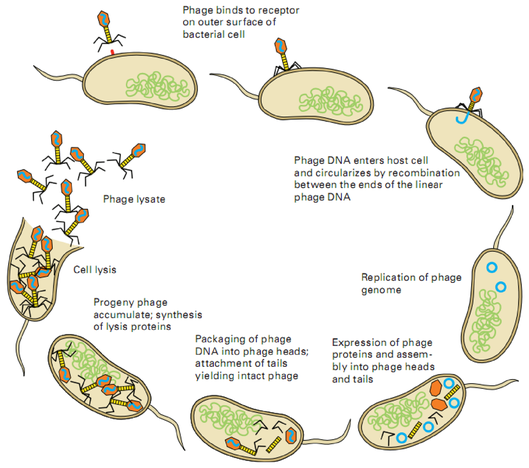

Figure 1. Sulakvelidze, Alavidze, & Morris, 2011, p. 654 Intralytix

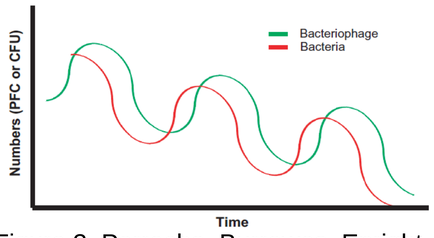

Figure 3. Parracho, Burrowes, Enright, McConville, & Harper, 2012, p. 283

Characteristics of a Good Phage for Therapy

- Bacteriophage identification
- Potency and biological activity of bacteriophages
- Control of sterility
- Manufacturing process considerations
- Lytic phages

(Parracho, Burrowes, Enright, McConville, & Harper, 2012)

Potential Problems

- Gene Transfer
- Changing Host range
- Antibiotic Resistance Transfer
- Identification o bacteria

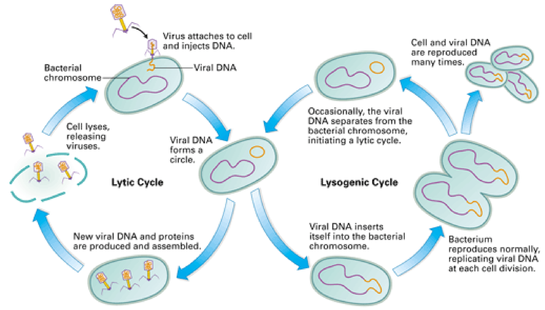

Figure 2. hbio3gbs1112.blogspot.com

Bacteriophages	Antibiotics	Comments
Very specific	Target all micro flora	High specificity can be disadvantageous
Replicate at the site of infection	Metabolized and eliminated from body	Exponential growth of phage may require fewer administrations
No serious side-effects described	Multiple side effects including allergies and secondary infections	Minor side effects of phage therapy may have been caused by release of endotoxins
Phage resistant bacteria remain susceptible to other phages with similar host range	Resistant to antibiotics not limited to targeted bacteria	Antibiotics select for many resistant bacterial species

Future Focus

“Concentrate on pathogens that represent the greatest problems with respect to antibiotic resistance like *staphylococci, enterococci, klebsiellae, and enterobacteria. Some Klebsiella pneumoniae* and *E. coli* isolates are already resistant against all known antibiotics and patients with these pathogens are doomed. Targeting these infections with phages might thus address a medical emergency.” (Brüssow, 2012, p. 141).

Future of Phage Therapy

Many studies of phage therapy are in different stages of production. There are available phage cocktail available from Microgen in Russia and the Eliavia Institute in Georgia where phage therapy is used as an over the counter drug. The Nestle Research company is currently studying these phage cocktails under double-blind, placebo controlled conditions (Brüssow, 2012). One study that is treating pseudomonas infections in the ear have research stage III clinical trials which are the last phase before distribution to the public (Wright, Hawkins, Änggård, & Harper, 2009).

One of the largest hurdle for phage therapy is the financial hurdle with new drugs costing $10-$50 million to create (Brüssow, 2012). Companies are unwilling to pursue phages as they cannot patent the phage itself. They can however patent the technology and techniques used to isolate and propagate their phage.

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